Wiskott-Aldrich syndrome

Wiskott-Aldrich syndrome is characterized by abnormal immune system function (immune deficiency) and a reduced ability to form blood clots. This condition primarily affects males.

Individuals with Wiskott-Aldrich syndrome have microthrombocytopenia, which is a decrease in the number and size of blood cells involved in clotting (platelets). This platelet abnormality, which is typically present from birth, can lead to easy bruising or episodes of prolonged bleeding following minor trauma.

Wiskott-Aldrich syndrome causes many types of white blood cells, which are part of the immune system, to be abnormal or nonfunctional, leading to an increased risk of several immune and inflammatory disorders. Many people with this condition develop eczema, an inflammatory skin disorder characterized by abnormal patches of red, irritated skin. Affected individuals also have an increased susceptibility to infection. People with Wiskott-Aldrich syndrome are at greater risk of developing autoimmune disorders, which occur when the immune system malfunctions and attacks the body's own tissues and organs. The chance of developing some types of cancer, such as cancer of the immune system cells (lymphoma), is also greater in people with Wiskott-Aldrich syndrome.

Frequency

The estimated incidence of Wiskott-Aldrich syndrome is between 1 and 10 cases per million males worldwide; this condition is rarer in females.

Genetic Changes

Mutations in the *WAS* gene cause Wiskott-Aldrich syndrome. The *WAS* gene provides instructions for making a protein called WASP. This protein is found in all blood cells. WASP is involved in relaying signals from the surface of blood cells to the actin cytoskeleton, which is a network of fibers that make up the cell's structural framework. WASP signaling activates the cell when it is needed and triggers its movement and attachment to other cells and tissues (adhesion). In white blood cells, this signaling allows the actin cytoskeleton to establish the interaction between cells and the foreign invaders that they target (immune synapse).

WAS gene mutations that cause Wiskott-Aldrich syndrome lead to a lack of any functional WASP. Loss of WASP signaling disrupts the function of the actin cytoskeleton in developing blood cells. White blood cells that lack WASP have a decreased ability to respond to their environment and form immune synapses. As a result, white blood cells are less able to respond to foreign invaders, causing many of

the immune problems related to Wiskott-Aldrich syndrome. Similarly, a lack of functional WASP in platelets impairs their development, leading to reduced size and early cell death.

Inheritance Pattern

This condition is inherited in an X-linked pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. In females (who have two X chromosomes), a mutation in one of the two copies of the gene in each cell may or may not cause the disorder. In males (who have only one X chromosome), a mutation in the only copy of the gene in each cell causes the disorder. In most cases of X-linked inheritance, males experience more severe symptoms of the disorder than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Other Names for This Condition

- eczema-thrombocytopenia-immunodeficiency syndrome
- IMD2
- immunodeficiency 2
- Wiskott syndrome

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Wiskott-Aldrich syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0043194/

Other Diagnosis and Management Resources

- GeneReview: WAS-Related Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK1178
- MedlinePlus Encyclopedia: Thrombocytopenia
  https://medlineplus.gov/ency/article/000586.htm
- National Marrow Donor Program
  https://bethematch.org/for-patients-and-families/learning-about-your-disease/wiskott-aldrich-syndrome/
- Rare Disease Clinical Research Network: Primary Immune Deficiency Treatment Consortium
  http://www.rarediseasesnetwork.org/cms/pidtc/Learn-More/Disorder-Definitions#WAS

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Thrombocytopenia
  https://medlineplus.gov/ency/article/000586.htm
- Health Topic: Bleeding Disorders
  https://medlineplus.gov/bleedingdisorders.html
- Health Topic: Eczema
  https://medlineplus.gov/eczema.html
- Health Topic: Immune System and Disorders
  https://medlineplus.gov/immunesystemanddisorders.html

Genetic and Rare Diseases Information Center

- Wiskott Aldrich syndrome
  https://rarediseases.info.nih.gov/diseases/7895/wiskott-aldrich-syndrome

Additional NIH Resources

- National Heart, Lung, and Blood Institute: Thrombocytopenia
  https://www.nhlbi.nih.gov/health/health-topics/topics/thcp/
- National Institute of Allergy and Infectious Diseases: Primary Immune Deficiency Diseases
  https://www.niaid.nih.gov/diseases-conditions/primary-immune-deficiency-diseases-pidds

Educational Resources

- Boston Children's Hospital: Autoimmune Diseases
  http://www.childrenshospital.org/conditions-and-treatments/conditions/a/autoimmune-diseases
- Boston Children's Hospital: Thrombocytopenia
  http://www.childrenshospital.org/conditions-and-treatments/conditions/thrombocytopenia
- Boston Children's Hospital: Wiskott-Aldrich Syndrome
  http://www.childrenshospital.org/conditions-and-treatments/conditions/w/wiskott-aldrich-syndrome
- Cleveland Clinic: Eczema
  http://my.clevelandclinic.org/health/articles/understanding-eczema
- Disease InfoSearch: Wiskott Aldrich syndrome
  http://www.diseaseinfosearch.org/Wiskott+Aldrich+syndrome/7514
- Immune Deficiency Foundation: Wiskott-Aldrich Syndrome
  http://primaryimmune.org/about-primary-immunodeficiencies/specific-disease-types/wiskott-aldrich-syndrome/
- MalaCards: wiskott-aldrich syndrome
  http://www.malacards.org/card/wiskott_aldrich_syndrome
- Orphanet: Wiskott-Aldrich syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=906

Patient Support and Advocacy Resources

- CLIMB: Children Living with Inherited Metabolic Diseases
  http://www.climb.org.uk/
- Immune Deficiency Foundation
  http://primaryimmune.org/
- Internation Patient Organisation for Primary Immunodeficiencies
  http://www.ipopi.org/
- National Organization for Rare Disorders (NORD): WAS Related Disorders
  https://rarediseases.org/rare-diseases/was-related-disorders/
- Platelet Disorder Support Association: Platelet Details
  https://www.pdsa.org/about-itp/platelet-details.html
- Rare Disease Clinical Research Network: Primary Immune Deficiency Treatment Consortium
  http://www.rarediseasesnetwork.org/cms/pidtc/Learn-More/Disorder-Definitions#WAS

- The Wiskott-Aldrich Foundation
  http://www.wiskott.org/
- University of Kansas Medical Center Resource List: Immune Deficiency Conditions
  http://www.kumc.edu/gec/support/immune.html

GeneReviews

- WAS-Related Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK1178

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Wiskott-Aldrich+syndrome%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Wiskott-Aldrich+syndrome%5BTI%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM

- WISKOTT-ALDRICH SYNDROME
  http://omim.org/entry/301000

Sources for This Summary

- Blundell MP, Worth A, Bouma G, Thrasher AJ. The Wiskott-Aldrich syndrome: The actin cytoskeleton and immune cell function. Dis Markers. 2010;29(3-4):157-75. doi: 10.3233/DMA-2010-0735. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21178275
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3835520/
- GeneReview: WAS-Related Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK1178
- Gulácsy V, Freiberger T, Shcherbina A, Pac M, Chernyshova L, Avcin T, Kondratenko I, Kostyuchenko L, Prokofjeva T, Pasic S, Bernatowska E, Kutukculer N, Rascon J, Iagaru N, Mazza C, Tóth B, Erdos M, van der Burg M, Maródi L; J Project Study Group. Genetic characteristics of eighty-seven patients with the Wiskott-Aldrich syndrome. Mol Immunol. 2011 Feb;48(5):788-92. doi: 10.1016/j.molimm.2010.11.013. Epub 2010 Dec 24.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21185603
- Lutskiy MI, Rosen FS, Remold-O'Donnell E. Genotype-proteotype linkage in the Wiskott-Aldrich syndrome. J Immunol. 2005 Jul 15;175(2):1329-36.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16002738
- Notarangelo LD, Miao CH, Ochs HD. Wiskott-Aldrich syndrome. Curr Opin Hematol. 2008 Jan; 15(1):30-6. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18043243

- Notarangelo LD, Ochs HD. Wiskott-Aldrich Syndrome: a model for defective actin reorganization, cell trafficking and synapse formation. Curr Opin Immunol. 2003 Oct;15(5):585-91. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14499269
- Ochs HD, Thrasher AJ. The Wiskott-Aldrich syndrome. J Allergy Clin Immunol. 2006 Apr;117(4): 725-38; quiz 739. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16630926
- Thrasher AJ. New insights into the biology of Wiskott-Aldrich syndrome (WAS). Hematology Am Soc Hematol Educ Program. 2009:132-8. doi: 10.1182/asheducation-2009.1.132. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20008191

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